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Radiosurgery: current recommendations for intracranial lesions and practices in pakistan

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RADIOSURGERY: CURRENT RECOMMENDATIONS FOR INTRACRANIAL LESIONS AND PRACTICES IN PAKISTAN

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ABSTRACT

Background: Radiosurgery is defined as the use of high-dose ionizing radiation for precise and total destruction of a chosen target, avoiding concomitant or delayed harm to adjacent tissues. The three types of radiations include gamma rays (GammaKnife) by Cobalt-60, X8 rays using linear accelerator (LINAC) system, and charged-particles generated from synchocyclotron. **Recommendations:** Based on current evidence, radiosurgery has proven benefits as the treatment of certain brain metastases, vestibular schwannomas, meningiomas, and some skull base tumors. **Conclusion:** This review describes the current recommendations for use of radiosurgery for intracranial pathologies. Radiosurgery is a relatively newer modality in the developing country of Pakistan. Much work is needed to increase awareness and promote its use as and when indicated.

Keywords: Radiosurgery, Current recommendations, Pakistan

INTRODUCTION

The term "radiosurgery" was coined by Prof. Lars Leksell from Karolinska Institute in Stockholm, Sweden. He defined radiosurgery as the use of a high-dose ionizing radiation for precise and total destruction of a chosen target, avoiding concomitant or delayed harm to the adjacent tissues [(1)]. He also described the use of stereotactic methods to develop the principles of radiosurgery in 1951 [(2)]. Since its advent, radiosurgery has come a long way to become an indication for treatment of a number of intracranial pathologies. One of the types of radiations involved in radiosurgery included the gamma rays, and was termed Gamma Knife. Gamma knife involves placement of a Leksell frame around the head of the patient for stereotactic localization of the brain lesion. This is followed by closed skull irradiation in a single-treatment session. The frame is used to fix the head of the patient, as multiple gamma ray beams focus at the chosen target. Cobalt-60 is used as the generation source [(3)]. Gamma Knife has evolved to become one of the indicated treatments for intracranial brain metastasis and vascular malformations [(4)]. Another type of ionizing beam used for radiosurgery involved 1 the Linear Accelerator (LINAC) system to generate high-speed photons, which subsequently produce X-rays focused at a desired target lesion. The LINAC system avoids the use of fixed frame; the patient lies in a steady position while the LINAC head moves around to focus the target through different arcs [(4)]. The LINAC system has been developed further for improved dose planning and dose distribution [(3, 4)]. Moreover, since it does not involve a fixed frame system, its use is extended to lesions outside the cranial cavity [(4)]. Charged-particle radiosurgery involve proton beams generated using synchrocyclotrons. Only few of these systems are available in United States, lacking popularity mostly because of its high installation and maintenance costs [(4)]. The objective of this article is to discuss the current recommendations for use of radiosurgeryin intracranial pathologies. We reviewed the latest literature to define the indications and relative indications for radiosurgery, and identify the cases where radiosurgery is not recommended. This article is also the first attempt to highlight the current practices of radiosurgery in the developing country, Pakistan. We interviewed the providers of stereotactic radiosurgery in Pakistan, as well as a few physicians at a tertiary care center in Pakistan, whofollow the patients before or after radiosurgical treatment for their intracranial diseases.

INDICATIONS

Brain Metastasis

Stereotactic radiosurgery (SRS) has shown survival rates comparable to surgical resection followed by whole-brain radiotherapy [(5)]. SRS can be used for single or multiple brain metastatic [(6)], for small lesions (less than 3-3.5cm) [(7)], for surgically inaccessible lesions [(5, 7)], and for radioresistent tumors like melanoma and renal cell carcinoma [(5, 6)].

Meningioma
SRS can be used a primary or adjuvant treatment for meningiomas that arise within the base of skull and have a high-surgical risk [8], SRS can also be used for recurrent skull base lesions [9]. Better tumor control rates have been observed for benign meningiomas (WHOGrade I – about 95% at 5 years) as compared to atypical (WHO Grade II – 60% at 5 years) ormalignant meningiomas (WHO Grade III – 10% at 5 years) [10].

Vestibular 1 Schwannoma (Acoustic Neuromas)
SRS is indicated for solitary vestibular schwannomas that are less than 30mm in cisternal diameter. Better outcomes are reported in such patients [11]. Treatment success rates of 78.2% to 86.9% have been calculated even after considering 17% to 30% natural growth rate of tumors without intervention [12].

Nonvestibular Schwannoma (Nonacoustic Schwannoma)
Radiosurgery has shown good outcomes for trigeminal (CN V), facial (CN VII) and jugular foramen (CN IX, X, XI) schwannomas [13, 14]; it can be used as a primary treatment for small to medium sized lesions, and as an adjuvant for residual lesions after large tumor resections [13-16].

GlomusJugulare
With good tumor control and lesser cranial nerve deficits (IX, X, XI) as compared to gross total resection [17, 18], stereotactic radiosurgery is indicated for elderly patients, for patients with serious medical conditions, and for residual or recurrent tumor [19-21].

Arteriovenous Malformations (AVMs)
Stereotactic radiosurgery has shown complete occlusion rates of 72-96% with small AVMs (up to 3ml) [22]. However, there is a notable risk of bleeding during the latent period following radiosurgery and before obliteration of the lesion. Management of larger AVMs continues to be challenging, and even though methods like Salvage Therapy (ST), Staged Volume Radiosurgery (SVR) and Hypofractionated Stereotactic Radiotherapy (HSRT) have been used to avoid higher complication rates [22], multimodality treatment approach with embolization, microsurgery and/or radiosurgery is recommended [23].

RELATIVE INDICATIONS

Pituitary Adenomas
Stereotactic radiosurgery may be used for small secreting pituitary adenomas that fail to respond to medical management, and when surgery is contra-indicated [24]. However, theremay be a delay before remission and/or side-effects of hypopituitarism [25]. Hypofractionatedstereotactic radiosurgery using cyber-knife may be used for non-functioning large tumors, to prevent neuroendocrine complications and visual pathway defects [26].

Gliomas
Even with significant risk of radiation complications [27, 28], the use of SRS is implicated in the treatment of high-grade gliomas as a boost after external beam radiotherapy (EBRT), or for small focal recurrences [29]. However, the evidence is ambiguous and further research isneeded in this area [27]. For low-grade gliomas, SRS may be used as an adjuvant to surgical resection for residual or recurrent lesions, or for surgically inaccessible tumors [27, 30].

Craniopharyngioma
Stereotactic radiosurgery has a role as a primary treatment for small tumors (<3cm) (31), for recurrent lesions [31-33], for patients who are not good candidates for surgery [31], and for large tumors after surgical decompression/ debulking or in the hypofractionated form [33-35].

Cavernous Hemangioma
SRS may be used to avoid operative complications of excessive bleeding or damage to adjacent structures [36, 37]. SRS may be a primary therapy for small to medium sized lesions confirmed on typical imaging [36, 38], or follow surgical resection for any residual tumor in cases of large hemangiomas [36, 38].

Hemangioblastoma
With a reasonable outcome of treatment, SRS has a role in management of small and solid hemangioblastomas [39, 40], and those that cannot be resected surgically [39-42].

Chordoma
SRS is implicated in the management of chordomas with reasonable local tumor control when used as an adjunct to surgical resection, for residual and recurrent lesions [43-46].

Chondrosarcoma
Duration of less than 6 months between diagnosis and radiosurgery, age greater than 40 years, and single or no prior surgical resection are the factors that predict good tumor control after stereotactic radiosurgery [19]. Noting that, SRS may have a role as an adjunct in select patients after maximal surgical resection [19, 47, 48].

Trigeminal Neuralgia
Gamma knife radiosurgery has shown poorer pain control outcomes as compared to radiofrequency ablation or microvascular decompression [49-52]. However, gamma knife radiosurgery avoids the operative complications [50-52], and 1 may be used for patients who

cannot undergo invasive procedures [50]. Other problems associated with gamma knife radiosurgery include the delayed affect on facial pain and complications of numbness and paresthesia, especially radiosurgery is performed multiple times [49, 52].

Movement Disorders (Essential Tremors, Parkinson's Disease, Multiple Sclerosis)

Gamma knife thalamotomy may improve tremors related to Parkinson's disease and essential tremors [53-56]. The problems associated with this treatment modality involve the delay in the clinical effect and the complications of sensory or motor impairments or speech difficulties that may manifest months after the procedure [57-59].

NOT RECOMMENDED

Brain metastases

Stereotactic radiosurgery is not recommended for lesions greater than 3.5-4cm in diameter ofthose associated with obstruction of CSF and hydrocephalus [5]. Moreover, SRS should not be used for patients who score less than 70 on KarnofskyPerformance Scale (KPS) or have an uncontrolled systemic malignancy [5].

Arteriovenous Malformations (AVMs)

Radiosurgery after embolization of arteriovenous malformations has not been recommended in the past [60-62]. However, recent data suggest that embolization before gamma knife radiosurgery may be used in some selected cases of large AVMs [63].

Meningioma

For lesions presenting with increasing neurological deficits, and for large superficial lesions, stereotactic radiosurgery has shown poorer outcomes and should not be used [8, 9].

Glioma

In case of newly diagnosed glioblastoma, SRS has no survival benefit if administered before fractionated radiotherapy [27].

Hemagioblastoma

SRS is not recommended for asymptomatic lesions [41], or those with cystic component [64].

INCONCLUSIVE 1 EVIDENCE (CONTROVERSIAL)

Cavernous Malformation

While, some studies have shown good outcome and regression of lesion after radiosurgery [65, 66], other studies have highlighted obvious morbidity risks with only limited benefits of this treatment modality [67, 68]. Overall, the use of radiosurgery for cavernous malformation remains controversial [66, 69].

Epilepsy

While stereotactic radiosurgery has shown benefits as a treatment modality for epilepsy due to focal lesions (tumors, arteriovenous malformations or cavernous malformations) [70, 71], there is a lack of evidence to adequately define its role in treatment of seizures secondary to hypothalamic hamartomas or mesial temporal lobe epilepsy; varying results of seizure control and complications have been reported (70, 72-75). In addition, there is a potential risk ofseizures in the initial months after radiosurgery, due to a delay in the anti-epileptic effect afterthis procedure [70, 71, 73, 74].

Movement Disorders (Bradykinesia, dyskinesia, rigidity)

Studies have shown varying improvement and complication outcomes after gamma knife pallidotomy for bradykinesia, dyskinesia and rigidity [57, 76-78]. Further studies are needed for definitive recommendations [57].

COMPLICATIONS

The complications of stereotactic radiosurgery could be of acute or chronic type, and maypresent years after the treatment. The risk of complications is dependant on the dose and target volume administered. Brain edema [79-81] and radiation-induced cerebral necrosis (radio-necrosis) [27, 80-83] are well-known complications of stereotactic radiosurgery, with a considerable risk of injury to the structures nearby (e.g. optic chiasm, facial nerve, etc.). Since there is a significant risk of such morbid complications, careful planning and administration of stereotactic radiosurgery is of utmost importance in any center where it is practiced. Moreover, vasculopathic complications such as aneurysm or varix formation, stenotic or occlusive vasculopathy, and development of secondary neoplasm have also beenobservered [84, 85].

PRACTICES IN PAKISTAN

Gamma Knife Radiosurgery

Gamma Knife Radiosurgery first came to Pakistan in May 2008 at the Neurospinal and Medical Institute at Karachi. It was shortly followed by the first LINAC system introduced at the same institute. Since its installation, 1700 cases of Gamma Knife, and 800 cases using the LINAC system have been performed. Majority of the procedures include Vestibular Schwannomas, Meningiomas, Pituitary Adenomas, Gliomas, and Arteriovenous-Malformations. Other cases such as Craniopharyngiomas, tumors of Pineal region, and Cavernous malformations have also been treated. Patients are mostly from

Sindh (including Karachi), followed by Punjab and Khyber Pakhtunkhwa. With the apparent advantage of shorter duration of treatment, and faster recovery, Gamma Knife is becoming increasingly popular among the patients. Nevertheless, its use must be limited to treat the pathologies as and when indicated. There is significant scope for further growth and development of Gamma Knife radiosurgery in Pakistan. Additional gamma knife systems, one in each province, would make this treatment more accessible for patients, and can improve the outcomes of diseases that are otherwise easily manageable in other parts of the world.

LINAC (CyberKnife) Radiosurgery

LINAC (CyberKnife) system was introduced in Pakistan even more recently than Gamma Knife. Patients' Aid Foundation, a non-governmental organization (NGO), helped install theCyberKnife system at Jinnah Postgraduate Medical Center (JPMC) in Karachi in 2011. Sinceits installation, 905 sessions have been given to 269 patients from all over the country, and abroad. The treatment is offered for various lesions in the brain and the rest of the body. Majority of the patients come from Sindh (including Karachi), followed by the rest of the provinces.

The intracranial pathologies for which CyberKnife has been used include Vestibular Schwannomas, Meningioma, Brain metastases, Arteriovenous malformations, Craniopharyngioma, Pituitary Adenoma, Trigeminal Neuralgia, Giant cell tumor, Ependymoma, Glomus tumors, and others. Extracranial lesions in the prostate, lymph node, liver and spine are also treated with CyberKnife Radiosurgery. Initial follow-up results have shown good outcomes with the use of CyberKnife. However, a longer follow-up would be required for substantial conclusions. 9

Room for improvement

Stereotactic radiosurgery in Pakistan is a fairly recent treatment modality as compared to its introduction and use in the developed parts of the world; there is a significant room for improvement in this field to provide better healthcare for the patients. Stereotactic radiosurgery requires a multi-disciplinary approach to evaluate the patient's disease, and manage it according to the best possible evidence. Additional equipment with experienced operators is needed in various cities across the country to make this treatment modality more accessible and improve the quality of care provided by the involved healthcare personnel.

Similarly, a good referral system will improve the follow-up of patients undergoing stereotactic radiosurgery, providing a means to monitor and utilize Gamma Knife and CyberKnife as one of the treatment options for indicated lesions.

CONCLUSION

With the advancement in neuro-imaging, stereotactic technology, and robotics, radiosurgery has become one of the key modalities in treatment of various intracranial pathologies. This review describes the current recommendations based on the most recent literature. With the ongoing research to make tumor cells more radiosensitive and healthy cells more radioresistent, additional applications of radiosurgery can be anticipated. Nevertheless,stereotactic radiosurgery is not free from complications; it is very important to carefully evaluate individual cases in a multi-disciplinary setting before using stereotactic radiosurgeryas a treatment modality, and administer the radiation in a strictly controlled fashion.

Concurrently, as compared to the developed parts of the world, radiosurgery is relatively a new concept in a developing country like Pakistan; there have been only less than 6 years of experience in Gamma Knife, and 2 years of experience in CyberKnife procedures. There is a dire need to spread awareness and form a good referral system, so patients can benefit from radiosurgery as and when indicated. Moreover, additional equipment is needed to make thistreatment more accessible for patients and improve the outcomes of otherwise manageable diseases.

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Dr. Hussain Shallwani: Study concept and design, data collection, data analysis, manuscript writing, manuscript review

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